Transformation of immunosuppressive mtKRAS tumors into immunostimulatory tumors by Nerofe and Doxorubicin

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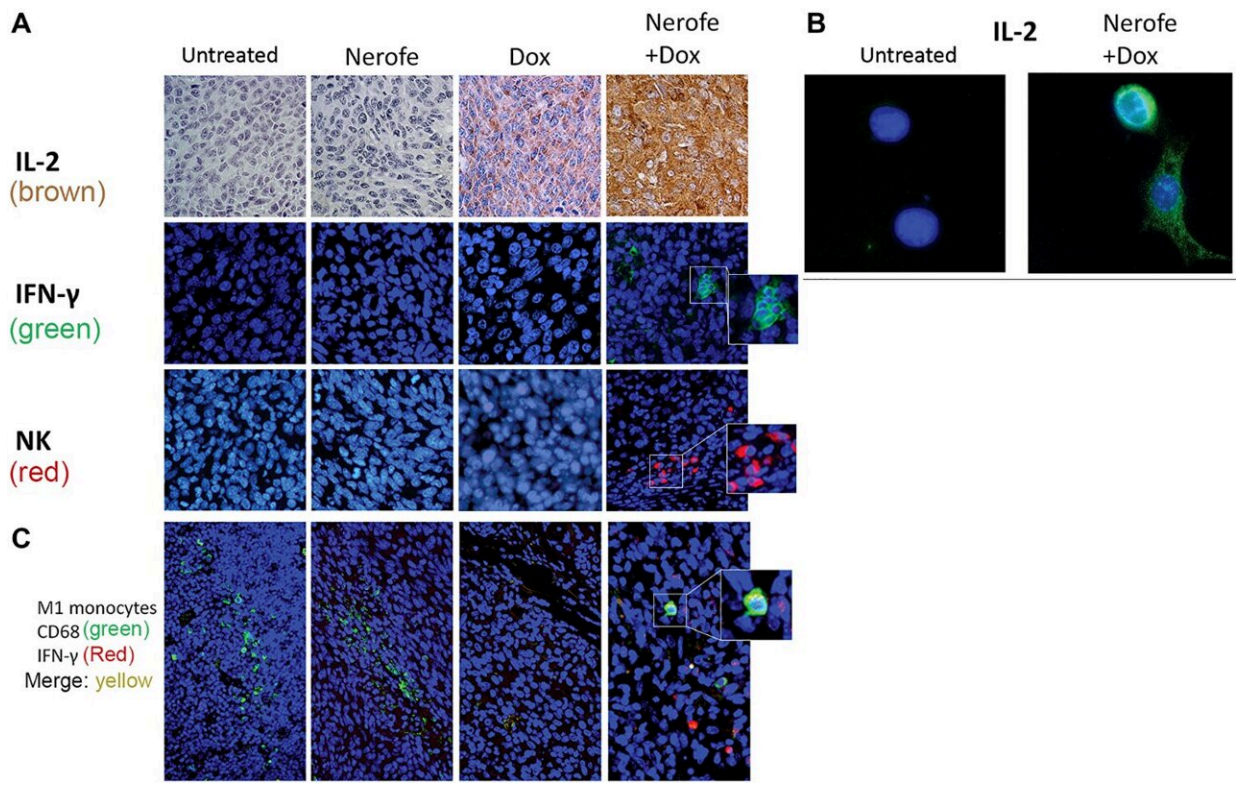

Immunological effect of Nerofe and DOX: CT26 murine model showing the immunological effect of Nerofe, DOX, and their combined treatment. Credit: 2023 Ohana et al.

A new research paper, titled "Transformation of immunosuppressive

mtKRAS tumors into immunostimulatory tumors by Nerofe and Doxorubicin," was published in *Oncotarget*

Members of the rat sarcoma viral oncogene (RAS) subfamily KRAS are frequently mutated oncogenes in human cancers and have been identified in pancreatic ductal, colorectal, and lung adenocarcinomas. Recently, two drugs that specifically target KRAS G12C, sotorasib (Lumakras) and adagrasib (Krazati), have received accelerated approval by the FDA for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic NSCLC, who have received at least one prior systemic therapy. These drugs are the first RAS GTPase family inhibitors to be approved for clinical use, representing a major breakthrough in the field of precision oncology.

In this new study, researchers Joel Ohana, Uziel Sandler, Orly Devary, and Yoram Devary from Immune System Key (ISK) and Jerusalem College of Technology show that a derivative of the hormone peptide Tumor Cell Apoptosis Factor (TCApF), Nerofe (dTCApFs), in combination with Doxorubicin (DOX) substantially reduces viability of tumor cells.

"The objective of the present study was to investigate the synergistic effect of the combination of Nerofe and DOX in colorectal cancer and its underlying mechanism," say the authors.

It was observed that the combination of Nerofe and DOX downregulated KRAS signaling via miR217 upregulation, resulting in enhanced apoptosis of tumor cells. In addition, the combination of Nerofe and DOX also resulted in activation of the immune system against tumor cells, manifested by an increase in the immunostimulatory cytokines IL-2 and IFN-γ as well as the recruitment of NK cells and M1 macrophages to the tumor site.

"In conclusion, we demonstrated that the combination of Nerofe and DOX exerts a synergistic effect during mCRC treatment, which could stem from several independent and complementary mechanisms of action," say the researchers.

More information: Joel Ohana et al, Transformation of immunosuppressive mtKRAS tumors into immunostimulatory tumors by Nerofe and Doxorubicin, *Oncotarget* (2023). DOI: 10.18632/oncotarget.28467

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